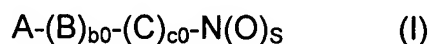


I. **AMENDMENTS TO THE CLAIMS:**

1. (Currently Amended) ~~Use for the preparation of disease-modifying drugs drugs~~  
~~for the prevention and treatment of~~ A method of preventing or reducing the  
degenerative effects on cartilaginous matrix comprising administering to a subject  
with arthritis therapy an effective amount of one or more compounds or salts  
thereof having the following general formula:



wherein:

s is an integer and is equal to 1 or 2, preferably 2;

c0 is an integer and is equal to 0 or 1;

b0 is an integer and is 0 or 1; with the proviso that at least one between of c0 and  
b0 is different from zero;

A = R-T<sub>1</sub>-, wherein

R- is the radical of a non steroidal antiinflammatory precursor drug  
excluding the compounds having 2-oxo-1H-indolic structure, or the radical  
of a non steroidal antiinflammatory/analgesic drug;

T<sub>1</sub> = (CO)<sub>t</sub> or (X)<sub>t'</sub>, wherein X = -O-, -S-, -N(R<sub>1C</sub>)-, R<sub>1C</sub> is H or C<sub>1</sub>-C<sub>5</sub> linear  
or branched alkyl, t and t' are integers and equal to zero or 1, with the  
proviso that t = 1 when t' = 0; t = 0 when t' = 1;

B = -T<sub>B</sub>-X<sub>2</sub>-T<sub>BI</sub>- wherein

T<sub>B</sub> and T<sub>BI</sub> are equal or different;

$T_B = (\text{CO})$  when the reactive function in the precursor drug is  $-\text{OH}$  or  $-\text{NH}(\text{R}_{1\text{C}})$ ;  $T_B = \text{X}$ , as above, when the reactive function in the precursor drug is  $-\text{COOH}$ ;

$T_{\text{BI}} = (\text{CO})_{\text{tx}}$  or  $(\text{X})_{\text{txx}}$ , wherein  $\text{tx}$  and  $\text{txx}$  have the value of 0 or 1; with the proviso that  $\text{tx} = 1$  when  $\text{txx} = 0$ ,  $\text{tx} = 0$  when  $\text{txx} = 1$ ;  $\text{X}$  is as above;

$\text{X}_2$  is a bivalent linking group as defined below;

$\text{C}$  is the bivalent radical  $-\text{T}_\text{C}-\text{Y}-$  wherein

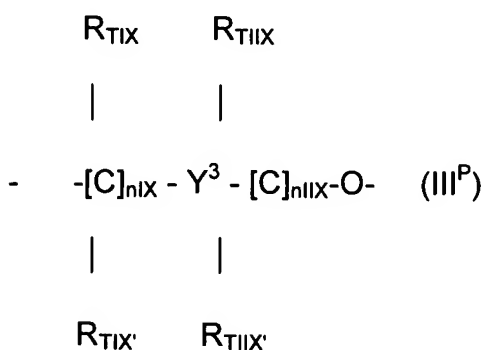
when  $b_0 = c_0 = 1$ :  $T_\text{C} = (\text{CO})$  when  $\text{tx} = 0$ ,  $T_\text{C} = \text{X}$  when  $\text{txx} = 0$ ,  $\text{X}$  being as above;

when  $b_0 = 0$ :  $T_\text{C} = (\text{CO})$  when  $t = 0$ ,  $T_\text{C} = \text{X}$  when  $t' = 0$ ,  $\text{X}$  being as above;

when  $c_0 = 0$ :  $\text{tx} = 0$ ,  $T_{\text{BI}} = \text{X} = -\text{O}-[\text{.}]_i$ ;

$\text{Y}$  is:

$\text{Y}_\text{p}$ :



wherein:

$\text{nIX}$  is an integer from 0 to 10, ~~preferably from 1 to 3~~;

$\text{nIIX}$  is an integer from 1 to 10, ~~preferably from 1 to 3~~;

$\text{R}_{\text{TIX}}$ ,  $\text{R}_{\text{TIX}'}$ ,  $\text{R}_{\text{TIIX}}$ ,  $\text{R}_{\text{TIIX}'}$ , equal to or different from each other are  $\text{H}$  or  $\text{C}_1\text{-C}_4$

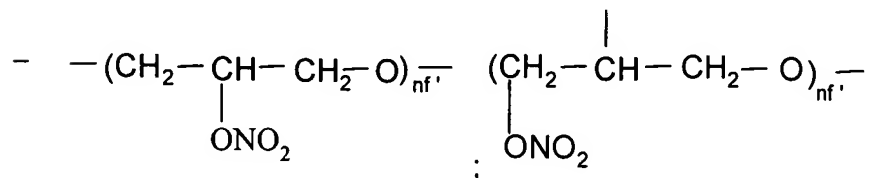
linear or branched alkyl; ~~preferably RTIX, RTIX', RTIIX, RTIIX' are H.~~

Y<sup>3</sup> is a saturated, unsaturated or aromatic heterocyclic ring containing one or two nitrogen atoms having 5 or 6 atoms,

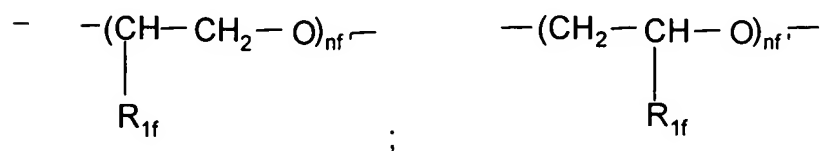
or Y can be:

Y<sub>0</sub>, selected from the following:

- a -R'O- alkyleneoxy group wherein R' is linear or branched when possible C<sub>1</sub>-C<sub>20</sub>, ~~preferably having from 2 to 6 carbon atoms~~, or a cycloalkylene having from 5 to 7 carbon atoms, in the cycloalkylene ring one or more carbon atoms can be substituted by heteroatoms, the ring can have side chains of R' type, R' being as above; or one of the following groups:

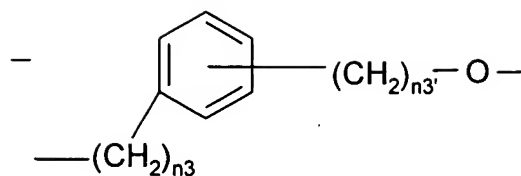


wherein n<sub>f</sub> is an integer from 1 to 6 ~~preferably from 1 to 4~~;

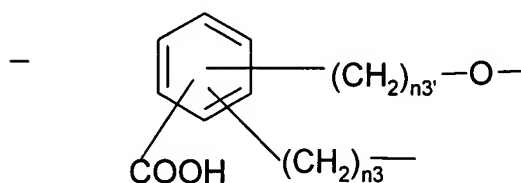


wherein R<sub>1f</sub> = H, CH<sub>3</sub> and n<sub>f</sub> is an integer from 1 to 6; ~~preferably from 1 to 4~~;

or Y is Y<sub>Ar</sub> and is selected from the following:



wherein  $n_3$  is an integer from 0 to 3 and  $n_{3'}$  is an integer from 1 to 3;



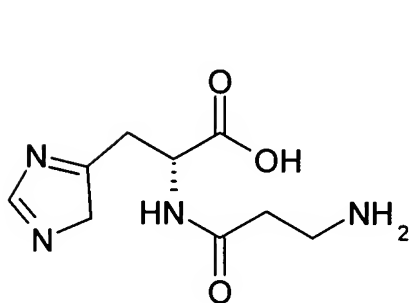
wherein  $n_3$  and  $n_{3'}$  have the above meaning;

$X_2$ , bivalent radical  $[[m]]$  is such that the corresponding precursor of B,  $-T_B-$   $X_2-T_{BI}-$  wherein the free valences of  $T_B$  and of  $T_{BI}$  are saturated each with OZ, with Z or with  $-N(Z^I)(Z^{II})$ , wherein  $Z = H$   $[[.]]$  or  $C_1-C_{10}$ , preferably  $C_4-C_5$  linear or branched when possible alkyl,  $Z^I$ ,  $Z^{II}$  equal or different have the Z values as above, depending on that  $T_B$  and/or  $T_{BI} = CO$  or X, in function of the values of t, t', tx and txx;

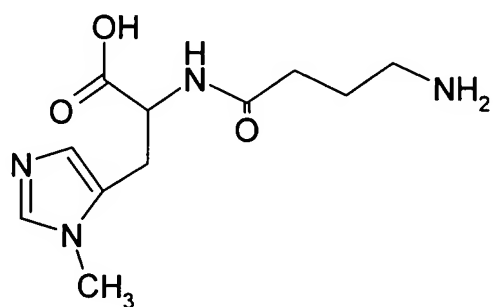
the precursor of B is selected from the following:

- aminoacids,
- hydroxyacids,
- aromatic and heterocyclic mono- and polyalchols,
- compounds containing at least one free acid function.

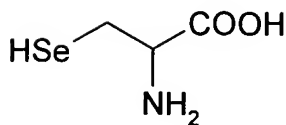
2. (Currently Amended) The method of Use according to claim 1, wherein the precursor of B is selected from the following: - aminoacids selected from the following: L-carnosine (formula CI), anserine (CII), selenocysteine (CIII), selenomethionine (CIV), penicillamine (CV), N-acetylpenicillamine (CVI), cysteine (CVII), N-acetylcysteine (CVIII), glutathione (CIX) or esters thereof, ~~preferably ethyl or isopropyl ester:~~



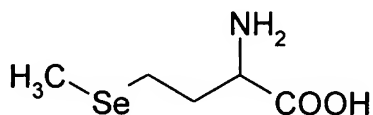
(CI)



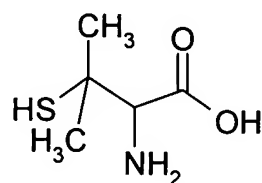
(CII)



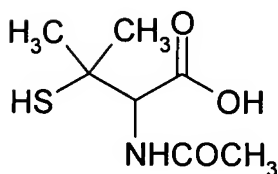
(CIII)



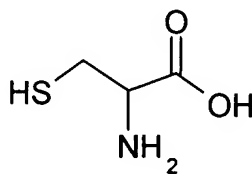
(CIV)



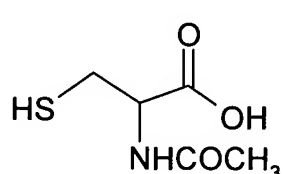
(CV)



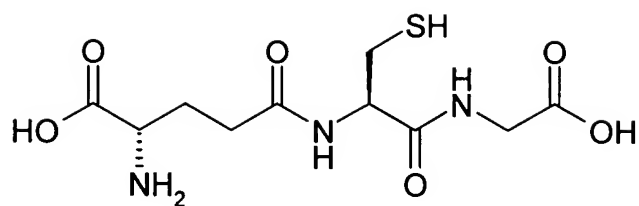
(CVI)



(CVII)

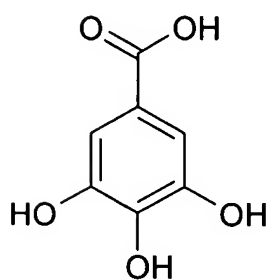


(CVIII)

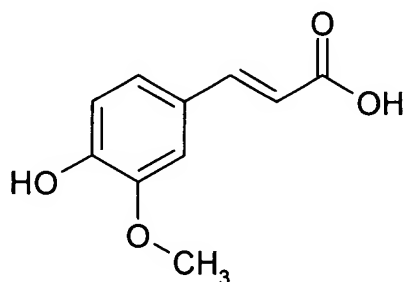


(CIX)

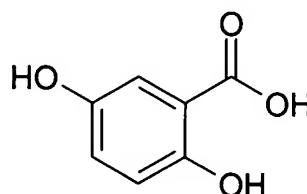
- hydroxyacids, selected from the following: gallic acid (formula DI), ferulic acid (DII), gentisic acid (DIII), citric acid (DIV), caffeic acid (DV), dihydrocaffeic acid (DVI), p-cumaric acid (DVII), vanillic acid (DVIII):



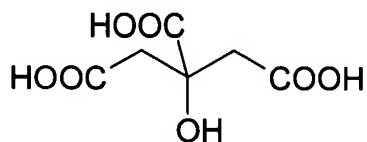
(DI)



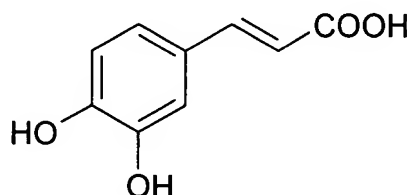
(DII)



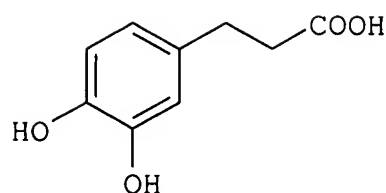
(DIII)



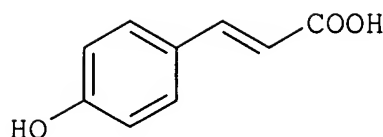
(DIV)



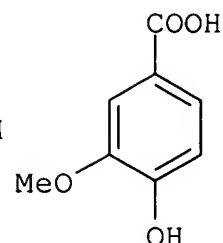
(DV)



(DVI)

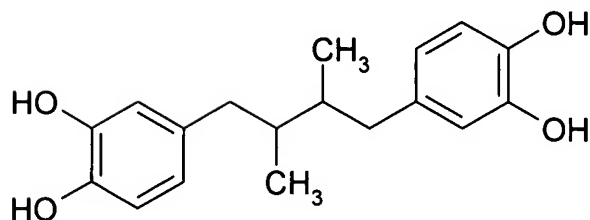


(DVII)

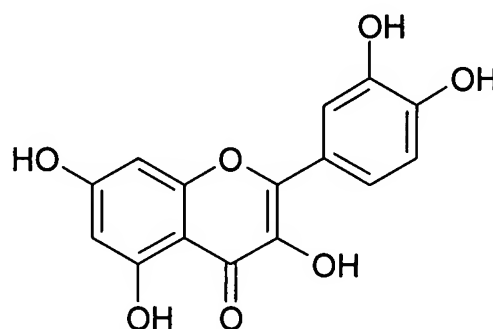


(DVIII)

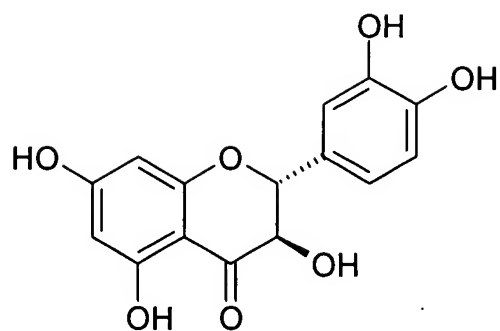
- aromatic and heterocyclic mono- and polyalcohols, selected from the following: nordihydroguaiaretic acid (EI), quercetin (EII), catekin (EIII), kaempferol (EIV), sulphurethyne (EV), hydroquinone (EVIII), gossypol (EIX), reductic acid (EX), methoxyhydroquinone (EXI), hydroxyhydroquinone (EXII), propyl gallate (EXIII), 3,5-di-ter-butyl-4-hydroxybenzyl-thioglycolate (EXXIV), allopurinol (EXXXI); saccharose (EC), ascorbic (ECI) and isoascorbic acid (ECII), p-cumaric alcohol (ECIII), 4-hydroxy-phenylethylalcohol (ECIV), coniferyl alcohol (ECV):



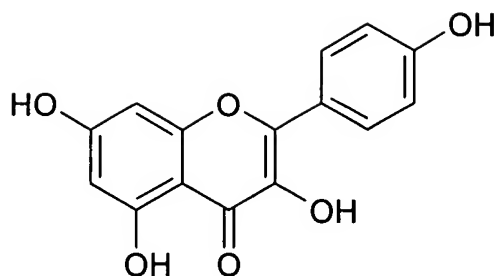
(EI)



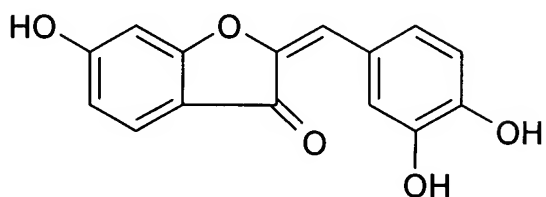
(EII)



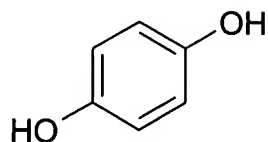
(EIII)



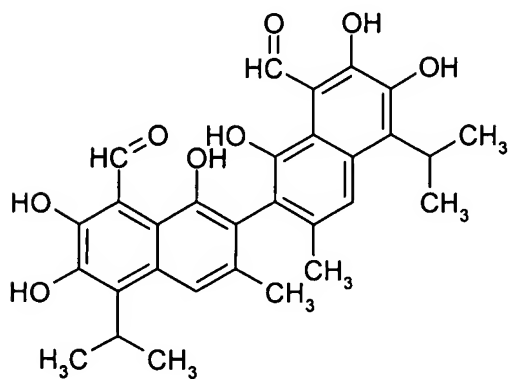
(EIV)



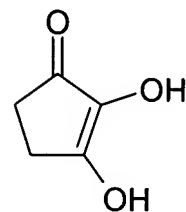
(EV)



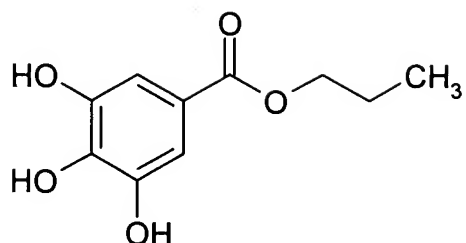
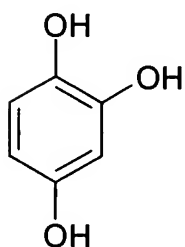
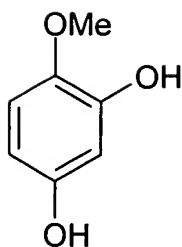
(EVIII)



(EIX)



(EX)

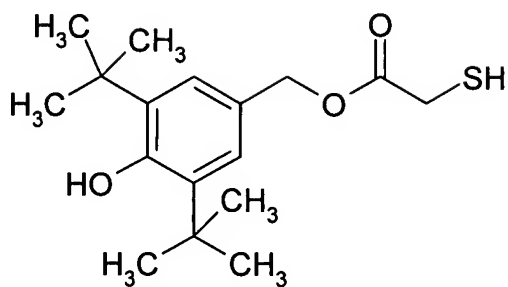




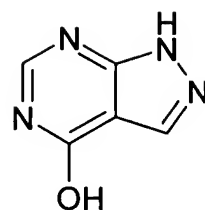
(EXI)

(EXII)

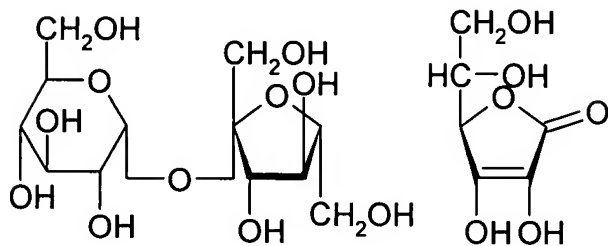
(EXIII)



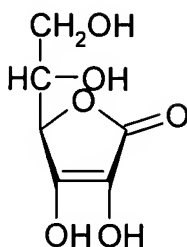
(EXXIV)



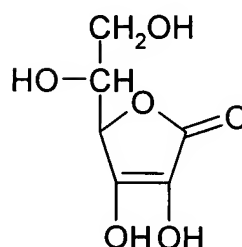
(EXXXI)



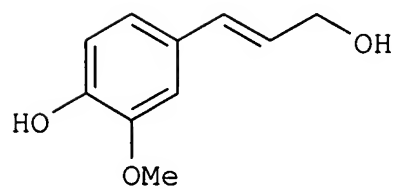
(EC)



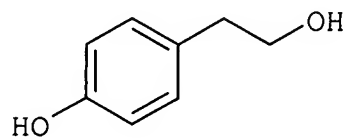
(ECI)



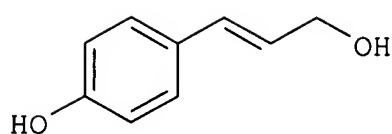
(ECII)



(ECIII)

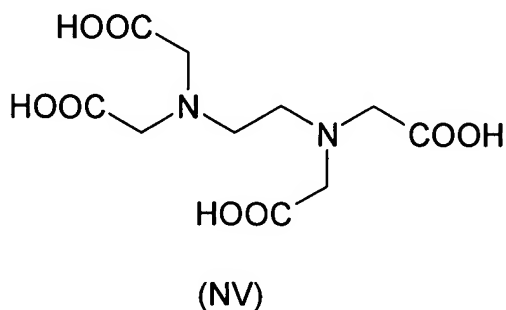


(ECIV)



(ECV)

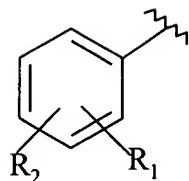
- OC(=O)CCSCCC(=O)O (NI)
 OC(=O)C=C(O)C(=O)O (NII)
 OC(=O)C(O)=C(O)C(=O)O (NIII)



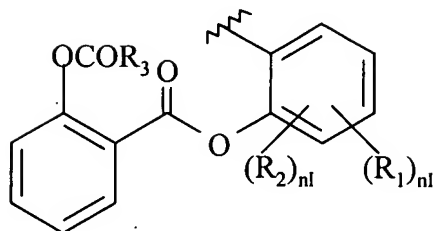
- TECH/548134.1

Group I)

la)



lb)



wherein:

$R_1$  is H or  $-OCOR_3$ ; wherein  $R_3$  is methyl, ethyl or  $C_3$ - $C_5$  linear or branched alkyl, or the residue of a heterocycle with only one ring having 5 or 6 atoms partially or totally hydrogenated, or aromatic, containing one or more heteroatoms independently selected from O, N and S;

$R_2$  is hydrogen, hydroxy, halogen,  $C_1$ - $C_4$  linear or branched alkyl,  $C_1$ - $C_4$  linear or branched alkoxy; a  $C_1$ - $C_4$  linear or branched perfluoroalkyl, for example trifluoromethyl; nitro, amino, mono- or di- $(C_{1-4})$  alkylamino;

with the proviso that in formula la)  $R_1$  and  $R_2$  are not contemporaneously H;

~~preferably when  $R_1 = H$   $R_2 = OH$ ;~~

~~preferably in the compounds of formula la)  $T_1 = CO$  and:~~

~~—  $R_1$  = acetoxy, preferably in ortho position with respect to  $\text{CO}$ ,  $R_2$  is hydrogen; in this case the formula Ia) represents the acetylsalicylic acid residue;~~

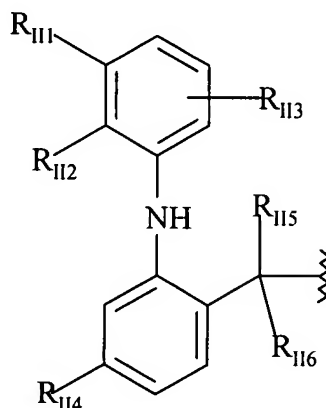
~~—  $R_1$  = H  $R_2$  = OH, preferably in ortho position with respect to  $\text{CO}$ , in this case the formula Ia) represents the salicylic acid residue;~~

in formula Ib)  $n_1$  is an integer 0 or 1;

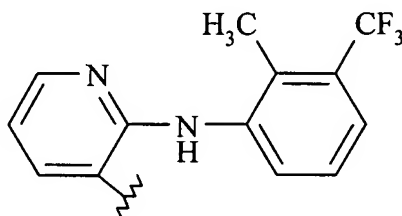
~~preferably in the compounds of formula Ib)  $R_3$  =  $\text{CH}_3$ ,  $n_1$  = 0,  $T_4$  =  $\text{CO}$ ; in this case Ib) is the acetylsalicylsalicylic acid residue;~~

Group II)

IIa)



IIb)



wherein:

R<sub>II5</sub> is H, C<sub>1</sub>-C<sub>3</sub> linear or branched ~~when possible~~ alkyl;

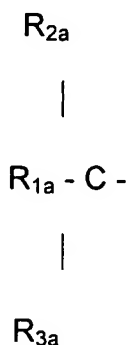
R<sub>II6</sub> has the same meaning as R<sub>II5</sub>, or when R<sub>II5</sub> is H it is benzyl;

R<sub>II1</sub>, R<sub>II2</sub> and R<sub>II3</sub> are independently hydrogen, C<sub>1</sub>-C<sub>6</sub> linear or branched alkyl, or C<sub>1</sub>-C<sub>6</sub> linear or branched alkoxy, or Cl, F, Br;

R<sub>II4</sub> is R<sub>II1</sub> or bromine;

~~the compounds are preferred wherein R<sub>II1</sub>, R<sub>II4</sub> are hydrogen and R<sub>II2</sub> and R<sub>II3</sub> are chlorine in ortho position with respect to NH; R<sub>II5</sub> and R<sub>II6</sub> are H, T<sub>1</sub> = -CO-, when the free valence is saturated with OH the precursor compound is known as diclofenac.~~

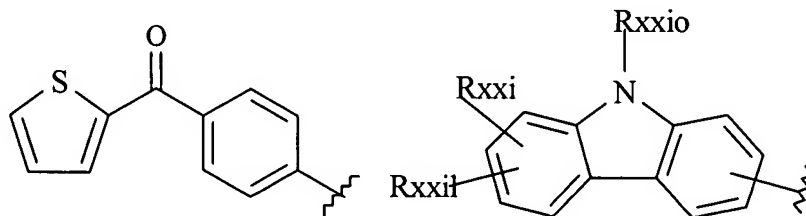
IIb) is the residue of the 2-[(2-methyl-3-(trifluoro methyl)phenyl)amino]-3-pyridincarboxylic acid when T<sub>1</sub> = -CO- and the free valence is saturated with OH the compound is known as flunixin;



wherein:

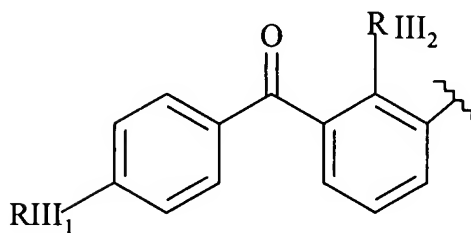
R<sub>2a</sub> and R<sub>3a</sub> are H, C<sub>1</sub>-C<sub>12</sub> linear or branched, substituted or not, alkyl or allyl, with the proviso that when one of the two is allyl the other is H; preferably ~~R<sub>2a</sub> and R<sub>3a</sub> equal or different, are H, C<sub>1</sub>-C<sub>4</sub> alkyl;~~

R<sub>1a</sub> is selected from:

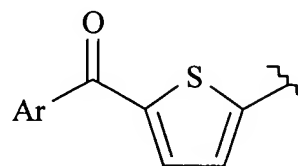


(II)

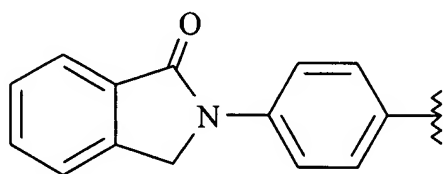
(XXI)



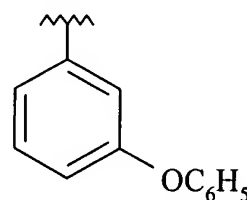
(IV)



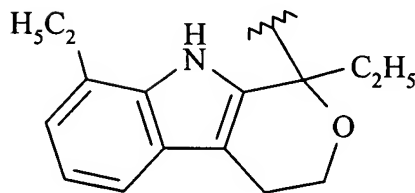
(XXXV)



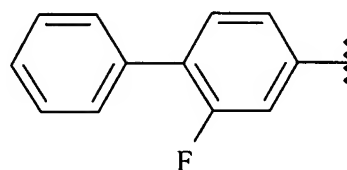
(VI)



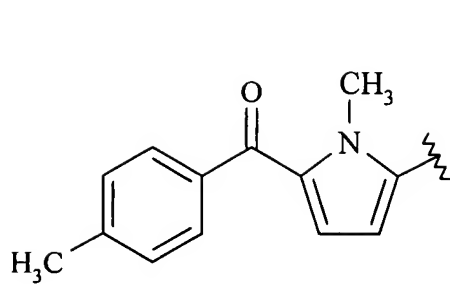
(VII)



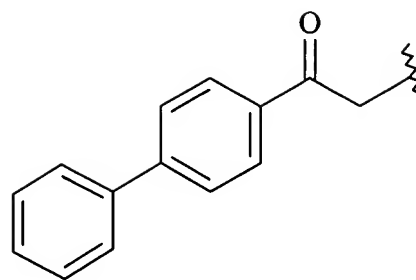
(VIII)



(IX)

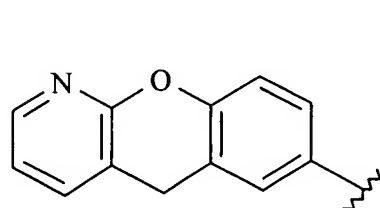


(X)

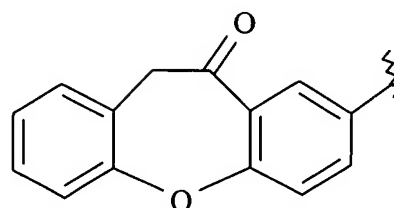


(III)

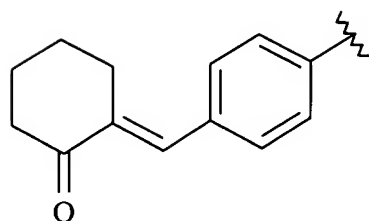
IIID) R<sub>1a</sub> corresponds to the following formulas:



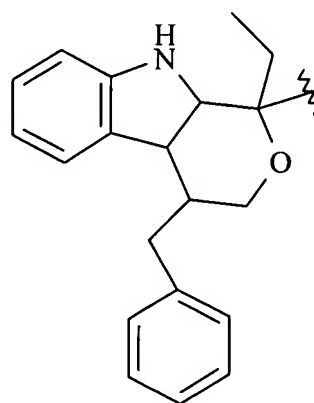
(IIIa)



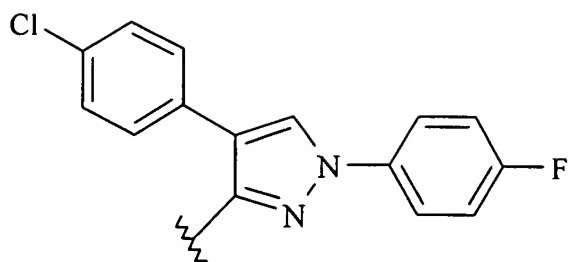
(XXX)



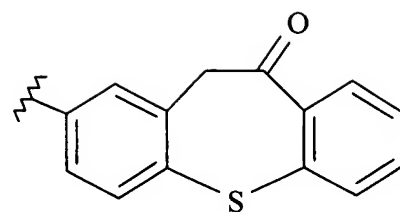
(XXXI)



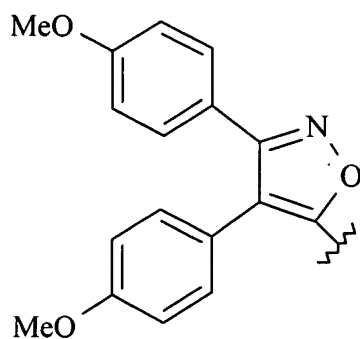
(XXXII)



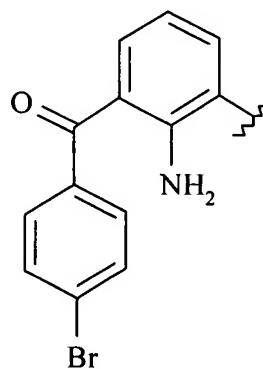
(XXXIII)



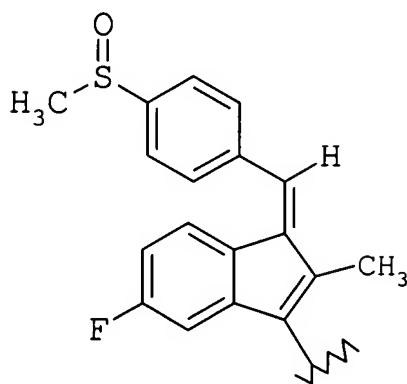
(XXXVI)



(XXXVII)



(XII)



(XXXX)

wherein the meanings are the following:

- when  $R_{1a}$  is as defined in formula (IV), Ketoprofen residue:



R<sub>III1</sub> is H, SR<sub>III3</sub> wherein R<sub>III3</sub> is C<sub>1</sub>-C<sub>4</sub> linear or branched alkyl;

R<sub>III2</sub> is H, hydroxy;

~~the compounds wherein R<sub>III1</sub> and R<sub>III2</sub> are H, R<sub>3a</sub> is H, and R<sub>2a</sub> is methyl, T<sub>1</sub> = CO are preferred;~~

- when R<sub>1a</sub> is as defined in formula (XXI), carprofen residue:

R<sub>xxio</sub> is H, alkyl from 1 to 6 C atoms linear or branched, C<sub>1</sub>-C<sub>6</sub>

alkoxycarbonyl linked to a C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> carboxyalkyl, C<sub>1</sub>-C<sub>6</sub> alkanoyl, optionally substituted with halogens, benzyl or halobenzyl, benzoyl or halobenzoyl;

R<sub>xxi</sub> is H, halogen, hydroxy, CN, C<sub>1</sub>-C<sub>6</sub> alkyl containing or not containing OH groups, C<sub>1</sub>-C<sub>6</sub> alkoxy, acetyl, benzyloxy, SR<sub>xxi2</sub> wherein R<sub>xxi2</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl; C<sub>1</sub>-C<sub>3</sub> perfluoroalkyl; C<sub>1</sub>-C<sub>6</sub> carboxyalkyl containing or not containing OH groups, NO<sub>2</sub>, amino; sulphamoyl, di-alkyl sulphamoyl with C<sub>1</sub>-C<sub>6</sub> alkyl, or difluoroalkylsulphonyl with C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sub>xxi1</sub> is halogen, CN, C<sub>1</sub>-C<sub>6</sub> alkyl containing one or more OH groups, C<sub>1</sub>-C<sub>6</sub> alkoxy, acetyl, acetamido, benzyloxy, SR<sub>III3</sub> being R<sub>III3</sub> as above, C<sub>1</sub>-C<sub>3</sub> perfluoroalkyl, hydroxy, C<sub>1</sub>-C<sub>6</sub> carboxyalkyl, NO<sub>2</sub>, amino, C<sub>1</sub>-C<sub>6</sub> mono- or di-alkyl-amino; sulphamoyl, C<sub>1</sub>-C<sub>6</sub> di-alkyl-sulphamoyl, or di-fluoroalkylsulphamoyl as above; or R<sub>xxi</sub> together with R<sub>xxi1</sub> is a C<sub>1</sub>-C<sub>6</sub> alkylene-dioxy;

OH groups, NO<sub>2</sub>, amino; sulphamoyl, di-alkyl sulphamoyl with C<sub>1</sub>-C<sub>6</sub> alkyl, or difluoroalkylsulphonyl with C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sub>xxi1</sub> is halogen, CN, C<sub>1</sub>-C<sub>6</sub> alkyl containing one or more OH groups, C<sub>1</sub>-C<sub>6</sub> alkoxy, acetyl, acetamido, benzyloxy, SR<sub>III3</sub> being R<sub>III3</sub> as above, C<sub>1</sub>-C<sub>3</sub> perfluoroalkyl, hydroxy, C<sub>1</sub>-C<sub>6</sub> carboxyalkyl, NO<sub>2</sub>, amino, C<sub>1</sub>-C<sub>6</sub> mono- or di-alkyl-amino; sulphamoyl, C<sub>1</sub>-C<sub>6</sub> di-alkyl-sulphamoyl, or di-fluoroalkylsulphamoyl as above; or R<sub>xxi</sub> together with R<sub>xxi1</sub> is a C<sub>1</sub>-C<sub>6</sub> alkylene-dioxy;

~~the compounds are preferred wherein R<sub>xxi0</sub> is H, the linking group is in position 2, R<sub>xxi</sub> is H, R<sub>xxi1</sub> is chlorine and is in para position with respect to the nitrogen;~~

~~R<sub>3a</sub> is H, R<sub>2a</sub> is methyl and T<sub>4</sub> = -CO-;~~

- when R<sub>1a</sub> is as defined in formula (XXXV) tiaprofenic acid residue:

Ar is phenyl, hydroxyphenyl optionally mono- or polysubstituted with halogen, alkanoyl and C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> trialkyl, preferably C<sub>4</sub>-C<sub>6</sub>, cyclopentyl, cyclohexyl, cycloheptyl, heteroaryl, preferably thienyl, furyl containing or not containing OH, pyridyl;

~~the preferred compounds of (XXXV) are those wherein Ar is phenyl, R<sub>3a</sub> is H, R<sub>2a</sub> is methyl and T<sub>1</sub> = -CO-;~~

- when R<sub>1a</sub> is as defined in formula (II), suprofen residue, R<sub>3a</sub> is H, R<sub>2a</sub> is methyl and T<sub>1</sub> = -CO-;

- when  $R_{1a}$  is as defined in formula (IX), R is the flurbiprofen residue when  $R_{3a} = H$ ,  $R_{2a} = CH_3$ ,  $T_1 = -CO-$ ;
- when  $R_{1a}$  is as defined in formula (X) R is the tolmetin residue when  $R_{2a} = R_{3a} = H$ ,  $T_1 = -CO-$ .

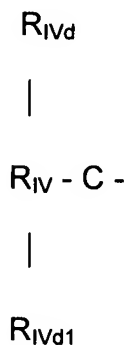
In group IIID)  $R_{1a}$  corresponds to the following formulas:

- IIIa), when  $R_{2a} = H$  and  $R_{3a} = CH_3$  the pranoprofen residue is obtained:  $\alpha$ -methyl-5H-[1]benzopyran-[2,3-b]pyridin-7-acetic acid; in the preferred compound  $R_{2a} = H$ ,  $R_{3a} = CH_3$ ,  $T_1 = -CO-$  and in the precursor the free valence is saturated with OH;
- (XXX), when  $R_{2a} = H$  and  $R_{3a} = CH_3$  the bermoprofen residue is obtained: dibenz[b,f]oxepin-2-acetic acid; in the preferred compound  $R_{2a} = H$ ,  $R_{3a} = CH_3$ ,  $T_1 = -CO-$ ;
- (XXXI), when  $R_{2a} = H$  and  $R_{3a} = CH_3$ , R is the radical of the compound CS-670: 2-[4-(2-oxo-1-cyclohexyliden methyl) phenyl]propionic acid; the preferred compound has  $R_{2a} = H$ ,  $R_{3a} = CH_3$ ,  $T_1 = -CO-$ ;
- (XXXII), when  $R_{2a} = R_{3a} = H$ , the pemedolac residue is obtained; when  $R_{2a} = R_{3a} = H$   $T_1 = -CO-$ ;
- (XXXIII), when  $R_{2a} = R_{3a} = H$ , the pirazolac residue is obtained: 4-(4-chlorophenyl)-1-(4-fluorophenyl)-3-pyrazol acid derivatives; the preferred compounds have  $R_{2a} = R_{3a} = H$ ,  $T_1 = -CO-$ ;
- (XXXVI), when  $R_{2a} = H$ ,  $R_{3a} = CH_3$  the zaltoprofen residue is obtained; when the residue is saturated with an hydroxyl or aminic group, or with the

carboxylic function the compounds are known as dibenzotiepin derivatives;  
in the preferred compounds  $R_{2a} = H$ ,  $R_{3a} = CH_3$ ,  $T_1 = -CO-$ ;

- (XXXVII), when  $R_{2a} = R_{3a} = H$  the mofezolac residue is obtained: 3,4-di(p-methoxyphenyl)isoxazol-5-acetic acid when the residue is  $CH_2-COOH$ ; in the preferred compounds  $R_{2a} = R_{3a} = H$ ,  $T_1 = -CO-$ ;
- (XII), when  $R_{2a} = R_{3a} = H$  the bromfenac residue is obtained: 2-amino-3-(4-bromobenzoyl)benzeneacetic acid; the preferred compounds have  $T_1 = -CO-$ ,  $R_{2a} = R_{3a} = H$ ;
- (XXXX) when  $R_{2a} = R_{3a} = H$  the sulindac residue is obtained: (Z)-5-fluoro-2-methyl-1-[[4-(methyl sulphinyl) -phenyl]methylene]-1H-inden-3-acetic acid; the preferred compounds have  $T_1 = -CO-$ ,  $R_{2a} = R_{3a} = H$ ;

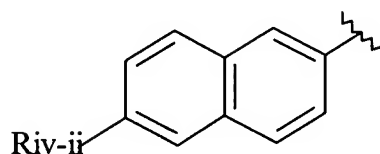
in Group IV) R is



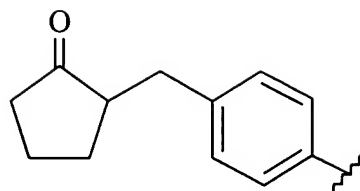
wherein:

$R_{IVd}$  and  $R_{IVd1}$  are at least one H and the other an alkyl from  $C_1$  to  $C_6$  linear or branched, preferably  $C_4-C_{27}$ , or difluoroalkyl with  $C_1-C_6$  alkyl,  $C_4$ -preferred, or  $R_{IVd}$  and  $R_{IVd1}$  form together a methylene group;

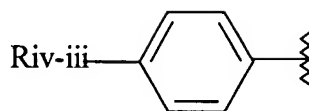
R<sub>IV</sub> has the following meaning;



(IIB)



(XB)



(IIIB)

wherein the compounds of group IV) have the following meanings:

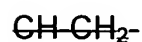
- in formula (IIB):

R<sub>IV-ii</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>1</sub>-C<sub>7</sub> alkoxymethyl, C<sub>1</sub>-C<sub>3</sub> trifluoroalkyl, vinyl, ethynyl, halogen, C<sub>1</sub>-C<sub>6</sub> alkoxy, difluoroalkoxy with C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>1</sub>-C<sub>7</sub> alkoxymethyloxy, alkylthiomethyloxy with C<sub>1</sub>-C<sub>7</sub> alkyl, alkyl methylthio with C<sub>1</sub>-C<sub>7</sub> alkyl, cyano, difluoromethylthio, phenyl- or phenylalkyl substituted with the C<sub>1</sub>-C<sub>8</sub> alkyl; preferably R<sub>IV-ii</sub> is CH<sub>3</sub>O-, R<sub>IVd</sub> is H and R<sub>IVd1</sub> is CH<sub>3</sub>, and is known as naproxene residue; T<sub>1</sub> = -CO-;

- in formula (XB), of which the loxoprofen residue has been indicated, the compounds wherein R<sub>IVd</sub> is H and R<sub>IVd1</sub> is CH<sub>3</sub>, T<sub>1</sub> = -CO- are preferred;
- in formula (IIIB):

$R_{IV-iii}$  is a  $C_2$ - $C_5$  branched or not branched alkyl,  $C_2$  and  $C_3$  alkyloxy, allyloxy, phenoxy, phenylthio, cycloalkyl from 5 to 7 C atoms, optionally substituted in position 1 by a  $C_1$ - $C_2$  alkyl;

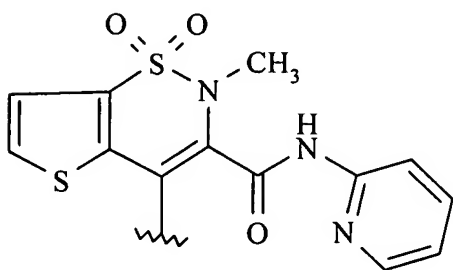
~~the compound is preferred wherein  $R_{IV-iii}$  is~~



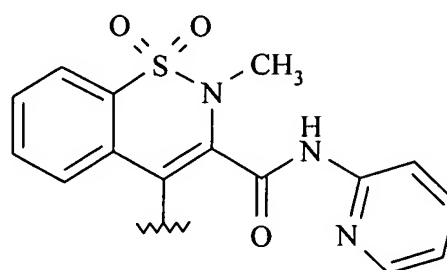
and  $R_{IVd} = H$ ,  $R_{IVd1}$  is  $CH_3$ , compound known as ibuprofen residue,  $T_1 = -$

$CO-$ ;

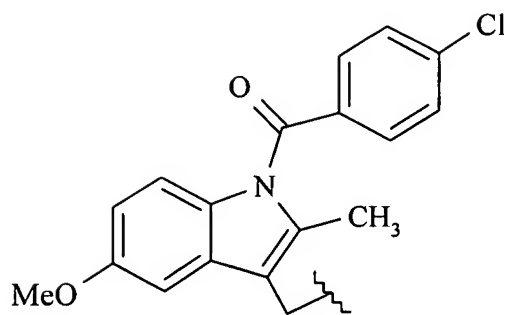
Group V)



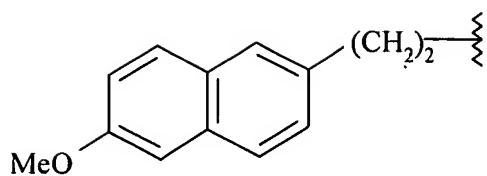
(VIIC)



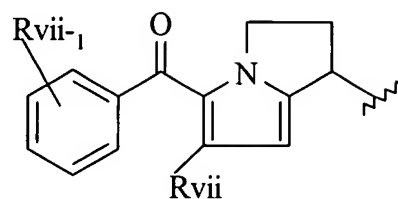
(IXC)



(IVC)

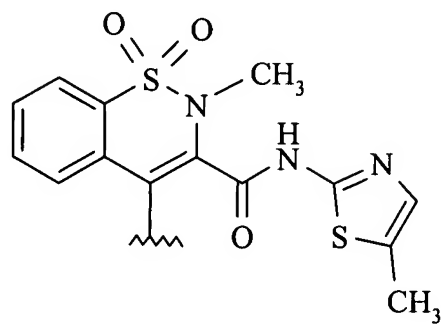


(IIIC)

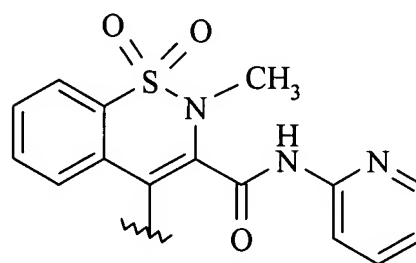


(IIC)

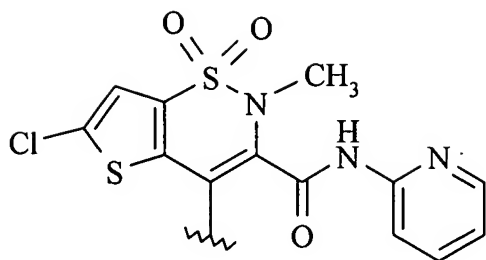
Group VE)



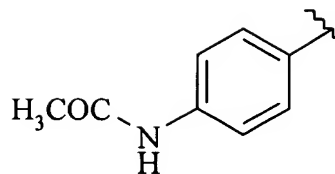
(XC)



(XI)



(XIII)



(XXXXV)

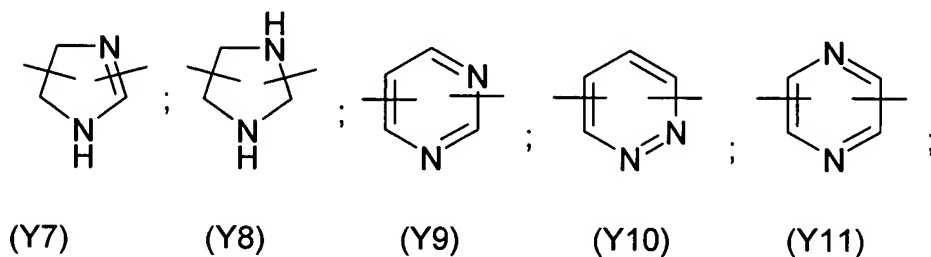
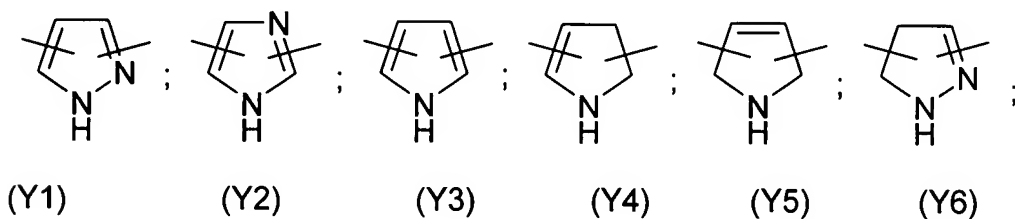
In group V), the compounds have the following meanings:

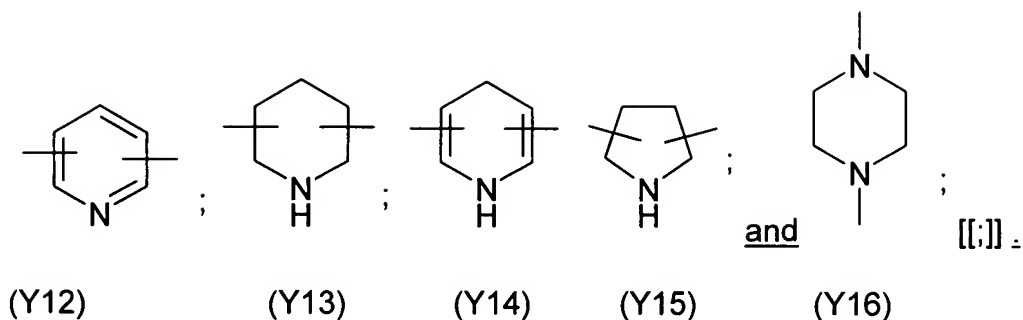
- when R is the formula (IIC),  
 $R_{VII}$  is H or a C<sub>1</sub>-C<sub>4</sub> linear or branched alkyl;  
 $R_{VII-1}$  is  $R_{VII}$ , or C<sub>1</sub>-C<sub>4</sub> linear or branched alkoxy; Cl, F, Br; the position of  $R_{VII-1}$  being ortho, or meta, or para;  
~~the Ketorolac residue is preferred, wherein  $R_{VII}$  and  $R_{VII-1}$  are H, and  $T_1 =$~~   
~~CO-~~;
- when R is the formula (VIIC),  
of which the tenoxicam residue has been indicated,  $T_1 = -O-$ ;
- when R is the formula (IXC),  
wherein  $T_1 = -O-$ , the piroxicam residue has been indicated;
- when R is the formula (IIIC),  
wherein  $T_1 = -CO-$ , of which the nabumetone residue has been indicated;
- when R is the formula (IVC),  
wherein  $T_1 = -CO-$ , of which the indomethacin residue has been indicated;
- when R is the formula (XC), the residue X is known as meloxicam; the preferred compounds are those in which  $T_1 = -CO-$ ;



- when R is the formula (XI) the residue is known as ampiroxicam when the termination is  $-\text{CH}(\text{CH}_3)\text{OCOC}_2\text{H}_5$ ; the preferred compounds have  $T_1 = -\text{CO}-$ ;
- when R is the formula (XIII) and the valence is saturated with H, the residue derives from lornoxicam; the preferred compounds have  $T_1 = -\text{O}-$ ;
- when R is the formula (XXXXV),  $T_1 = -\text{O}-$  and the valence is saturated with H, the compound known as paracetamol is obtained.

5. (Currently Amended) The method of Use according to claim 1, wherein in the compounds of formula (I)  $\text{Y}^3$  of formula (III<sup>P</sup>) of C is selected from the following bivalent radicals:





6. (Currently Amended) The method of Use according to claim 5, wherein  $Y^3$  is selected from the following: (Y12) with the two free valences in the ortho positions with respect to the nitrogen atom; (Y16) with the two valences linked to the two heteroatoms, Y1 (pyrazol) 3,5-disubstituted ; ~~Y16 is particularly preferred.~~

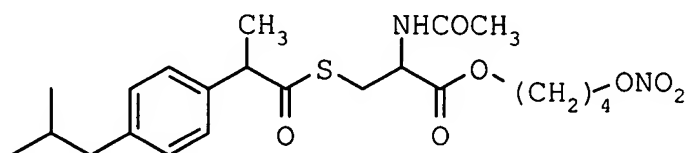
7. (Currently Amended) Use according to The method of claim 1, wherein the compounds or salts thereof of formula (I) are selected from the group consisting of: the following compounds are used:

2-acetyloxybenzoic acid 3-nitrooxymethyl phenyl ester (I<sup>C</sup>);

2-fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 4-nitrooxy butylester (II<sup>C</sup>);

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-nitrooxy butyl ester (III<sup>C</sup>);

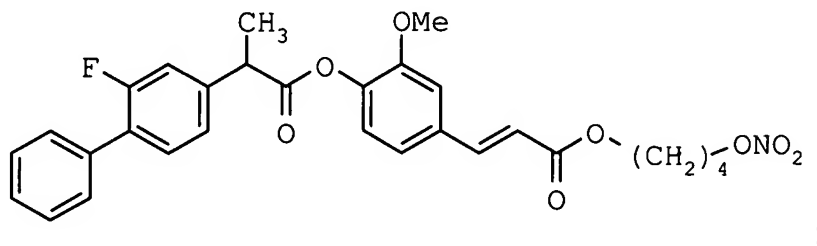
(S)-N-acetyl-[alpha-methyl-4-(2-methylpropyl)benzen-acetyl] cysteine 4-nitrooxybutylester having formula:



(IV<sup>C</sup>)

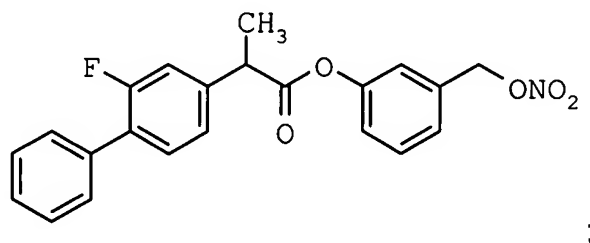
4-nitrooxybutanoic acid 4-acetylaminophenylester (V<sup>C</sup>);

trans-3-[4-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyloxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy) butyl ester, having formula:



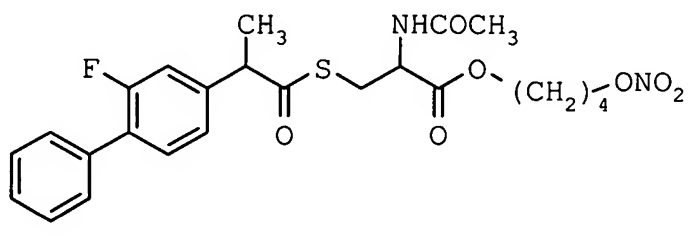
(VI<sup>C</sup>)

2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 3-(ni-trooxymethyl)phenyl ester having formula:



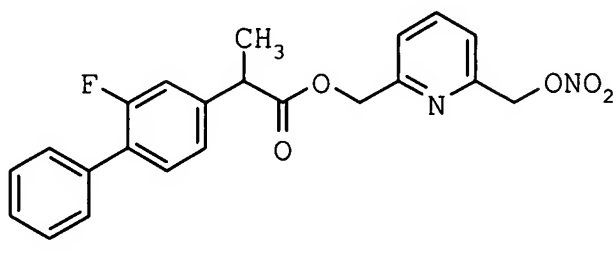
(VII<sup>C</sup>)

(S)-N-acetyl-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyl] cysteine 4-(nitrooxy)butyl ester having formula:



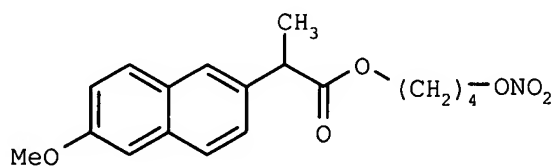
(VIII<sup>C</sup>)

2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 6-(nitrooxy methyl)-2-methylpyridyl ester having formula



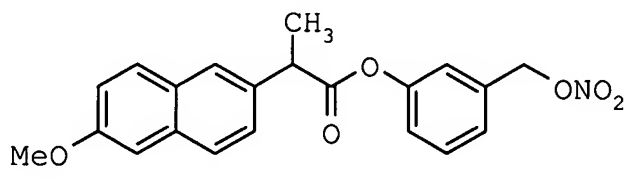
(XI<sup>C</sup>)

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 4-(nitrooxy)butyl ester having formula :



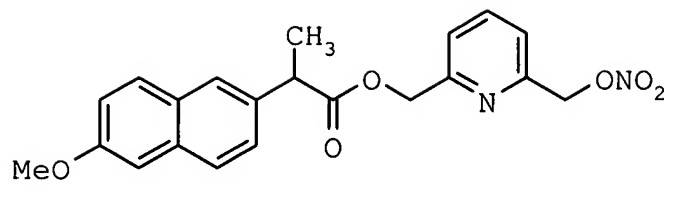
(X<sup>C</sup>);

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 3-(nitrooxymethyl)phenyl ester having formula:



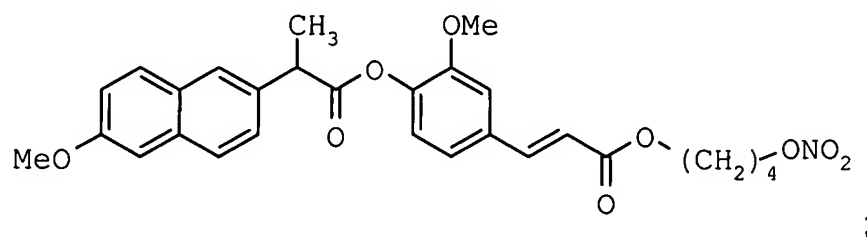
(XI<sup>B</sup>)

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl ester having formula:



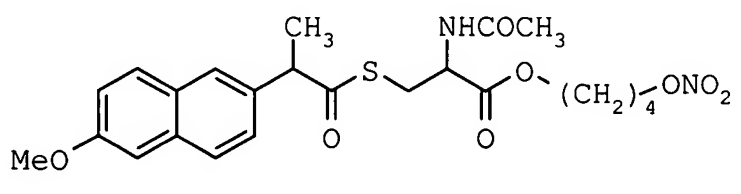
(XII<sup>c</sup>)

trans-3-[4-[6-methoxy-alpha-methyl-2-naphthalenyl acetyl oxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy)butyl ester having formula:



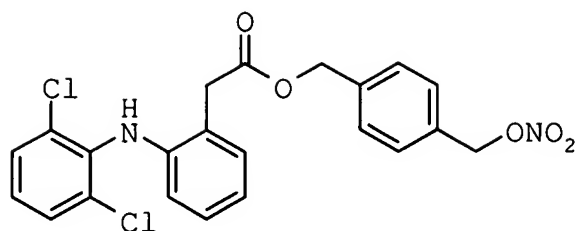
(XIII<sup>c</sup>)

(S,S)-N-acetyl-S-(6-methoxy-alpha-methyl-2-naphthaleneacetyl) cysteine 4-(nitrooxy)butyl ester having formula:



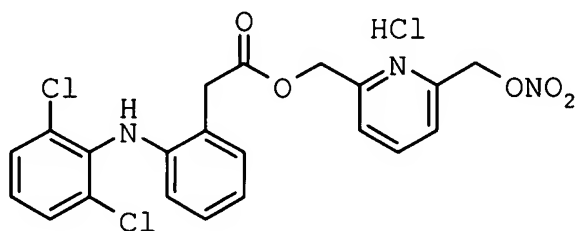
(XIV<sup>c</sup>)

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-(nitrooxy methyl)phenylmethyl ester having formula:



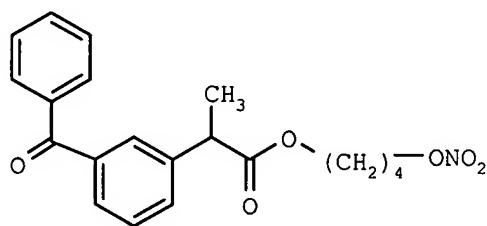
(XV<sup>c</sup>)

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl hydrochloride ester having formula:



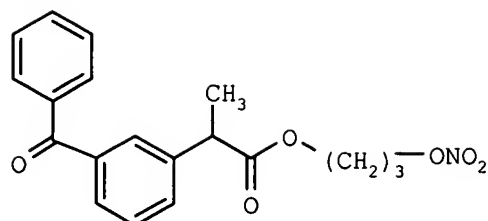
(XVI<sup>c</sup>)

(S)-3-benzoyl-alpha-methyl-benzenacetic acid 4-(nitro oxybutyl) ester having formula:



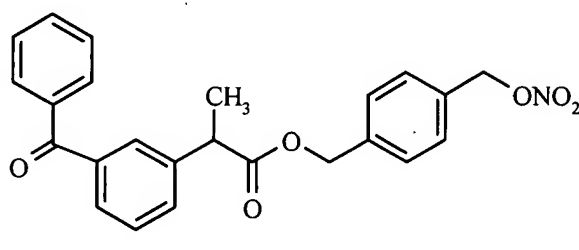
(XVII<sup>c</sup>)

(S)-3-benzoyl-alpha-methyl-benzenacetic acid 3-(nitro oxypropyl) ester having formula:



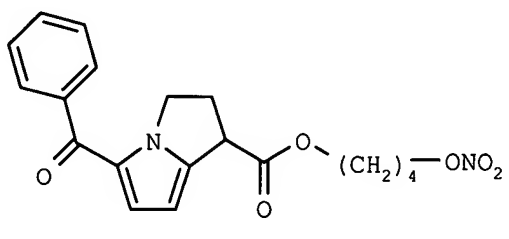
(XVIII<sup>c</sup>)

(S)-3-benzoyl- $\alpha$ -methyl-benzenacetic 4-(nitro oxymethyl) phenylmethyl ester  
having formula:



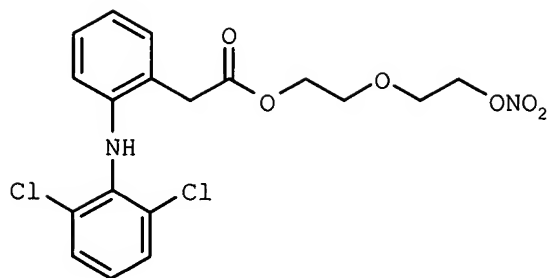
(XIX<sup>c</sup>)

5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid 4-(nitrooxy)butyl ester  
having formula:



(XXI<sup>c</sup>)

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 5 (nitro oxy)ethyloxyethyl ester  
having formula:



(XX<sup>C</sup>)

1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid 3-(nitrooxymethyl)phenyl ester (XXI<sup>C</sup>).

8. (Currently Amended) The method of Use according to claim 1, wherein the compounds or salts thereof of formula (I) are administered ~~in pharmaceutical formulations~~ by oral, parenteral ~~[[and]]~~ or topical administration.
9. (Currently Amended) The method of Use according to claim 1, wherein for the prevention of arthritis relapses of degenerative effects on cartilaginous matrix in subjects with arthritis are prevented.